| A. CLASSIFI   | CATION OF SUBJECT MATTER<br>C12N15/86  |  | ļ                        |
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| 110 /         | •  |  |                          |
|               | nternational Patent Classification (IPC) or to both national classification ar   | nd IPC   |                          |
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| Minimum doc   | umentation searched (classification system followed by classification system)  | bols)  |                          |
| IPC 7         | C12N   |  |                          |
|               | on searched other than minimum documentation to the extent that such do  | cuments are included in the fields sea   | rched                    |
| Documentation | on searched other than minimum documentation to the extent that  |  |                          |
|               | ta base consulted during the international search (name of data base and   | where practical, search terms used)  | · ••                     |
| Electronic da | ta base consulted during the international search (name of data search ( | ,  |                          |
| EPO-Int       | ternal, BIOSIS, MEDLINE, WPI Data, PAJ   | •  |                          |
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| C. DOCUME     | NTS CONSIDERED TO BE RELEVANT  Citation of document, with indication, where appropriate, of the relevant   | passages   | Relevant to claim No.    |
| Category °    | Citation of document, with indication, Whole appropriate   |  |                          |
| V             | GAO GUANGPING ET AL: "Adeno-associ   | ated   | 1-3,7                    |
| X             | l  | OH HII   |                          |
|               | primates during natural infections. PROCEEDINGS OF THE NATIONAL ACADEMY  | •  |                          |
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|               | vol. 100, no. 10,<br>13 May 2003 (2003-05-13), pages 608   | 31-6086  |                          |
|               | 13 May 2003 (2003-05-13), pages 300<br>XP002255703   | ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,  |                          |
|               | May 13 2003 2003   |  |                          |
|               | ISSN: 0027-8424  |  |                          |
|               | paragraph - right-hand column, par   | agraph   |                          |
|               | 1; figure 2A -/  |  |                          |
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| X F           | orther documents are listed in the continuation of box C.  | Patent family members are listed   | d in annex.              |
|               | categories of cited documents :  | later document published after the in  | sternational filing date |
|               | and defining the general state of the art which is not   | or priority date and not in conflict wi<br>cited to understand the principle or<br>invention   |                          |
|               | ment defining the script and scri | decument of particular relevance; the cannot be considered novel or cannot be considered novel o | claimed invention        |
| ilin filin    | g date   | involve an inventive step when the   | a claimed invention      |
| . whi         | ch is cited to establish the place specified)  | cannot be considered to involve an   | more other such docu-    |
| "O" doc       | ment referring to an oral disclosure, use, exhibition of   | ments, such combination being obtain the art.  | rious to a person simos  |
| doc           | ment published prior to the international filing date but<br>ar than the priority date claimed   | &" document member of the same pate  |                          |
|               | he actual completion of the international search   | Date of mailing of the international s   | earch report             |
|               | · ·  | 0 3 05   | 2005                     |
|               | 13 December 2004   | Authorized officer   |                          |
| Name a        | nd mailing address of the ISA<br>European Patent Office, P.B. 5818 Patentlaan 2  |  |                          |
|               | NL - 2280 HV Rijswijk<br>Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  | Niebuhr-Ebel, K  |                          |
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Interceptional Application No PCT/EP2004/006222

|            | 7   | PCT/EP2004/006 |             |
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| Continual  | lion) DOCUMENTS CONSIDERED TO BE RELEVANT   |                | <del></del> |
| Category ° | Citation of document, with indication, where appropriate, of the relevant passages  | Relevant       | o daim No.  |
| x ·        | & DATABASE SWALL EMBL; 1 June 2003 (2003-06-01), GAO ET AL.: "Adeno-associated viruses undergo substantial evolution in primates during natural infections" XP002255706 Database accession no. Q808Y0 the whole document  | 1              | -3,7        |
| <b>X</b>   | WO 02/053703 A (CHILDRENS HOSPITAL INC) (11 July 2002 (2002-07-11)  "AAV vectors and methods" page 20; example 3; table 4 claims 4,6,7  |                | ,6-10       |
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| P,X        | KERN A ET AL: "Identification of a heparin-binding motif on adeno-associated virus type 2 capsids."  JOURNAL OF VIROLOGY, vol. 77, no. 20, October 2003 (2003-10), pages 11072-11081, XP002310361 ISSN: 0022-538X the whole document  |                |             |
| P,X        | WO 03/054197 A (BUENING HILDEGARD; HUTTNER NADJA (DE); MEDIGENE AG (DE); PERABO LU) 3 July 2003 (2003-07-03) "A library of modified structural genes or capsid modified particles useful for the identification of viral clones with desired cell tropism" page 35; example 5 claims 13,41,42; table 1                                |                | 1,6-10      |
| . 6        | -/  |                | •           |

International Application No PC1/EP2004/006222

|            | <u> </u>  | PC17EP2004/006222 |                       |  |
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|            | INION) DOCUMENTS CONSIDERED TO BE RELEVANT  | <del></del> 1     | Relevant to claim No. |  |
| Category * | Citation of document, with indication, where appropriate, of the relevant passages  |                   | TOUTEN TO COMMITTEE   |  |
| P,X        | OPIE SHAUN R ET AL: "Identification of amino acid residues in the capsid proteins of adeno-associated virus type 2 that contribute to heparan sulfate proteoglycan binding."  JOURNAL OF VIROLOGY, vol. 77, no. 12, 20 June 2003 (2003-06-20), pages 6995-7006, XP009018010 ISSN: 0022-538X |                   | 1-10                  |  |
| ·.         | the whole document  |                   |                       |  |
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| Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).  Sox III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)  This International Searching Authority found multiple inventions in this international application, as follows:  see additional sheet  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.   | Box II Observations where certain claims were found unsearchable (Continuation of Item 2 of first sheet)  |
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| Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful international Search can be carried out, specifically:  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).  Sox III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)  International Searching Authority found multiple inventions in this international application, as follows:  See additional sheet  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:  As only some of the required additional search fees were paid, specifically claims Nos.:  As only some of the required additional search fees were paid, specifically claims Nos.:  As only some of the required additional search fees were paid, specifically claims Nos.:  As only some of the required additional search fees were paid, specifically claims Nos.:  As only some of the required additional search fees were paid, specifically claims Nos.:  As only some of the required additional search fees were paid, specifically claims Nos.:  By Only Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  By Only Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: | his International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:   |
| Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).  Loss III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)  This International Searching Authority found multiple inventions in this international application, as follows:  see additional sheet  Loss all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:  As only some of the required additional search fees were timely paid by the applicant, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  1-10  Remark on Protest  The additional search fees were accompanied by the applicant's protest.  | Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:   |
| Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).  Loss III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)  This International Searching Authority found multiple inventions in this international application, as follows:  see additional sheet  Loss all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:  As only some of the required additional search fees were timely paid by the applicant, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  1-10  Remark on Protest  The additional search fees were accompanied by the applicant's protest.  |   |
| Dox III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)  his International Searching Authority found multiple inventions in this international application, as follows:  see additional sheet  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:  A  | Claims Nos.:  because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: |
| see additional sheet  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  1-10  Remark on Protest  The additional search fees were accompanied by the applicant's protest.   | Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).  |
| see additional sheet  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  1-10  Remark on Protest  The additional search fees were accompanied by the applicant's protest.   | Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)  |
| As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which lees were paid, specifically claims Nos.:  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  1-10  Remark on Protest  The additional search fees were accompanied by the applicant's protest.   |   |
| As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.  3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:  4. X No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:   | see additional sheet  |
| As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  1-10  Remark on Protest  The additional search fees were accompanied by the applicant's protest.   | 1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.   |
| A. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:  1-10  Remark on Protest  The additional search fees were accompanied by the applicant's protest.  | 2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.   |
| 1-10  Remark on Protest  The additional search fees were accompanied by the applicant's protest.   | As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:                        |
| 1-10  Remark on Protest  The additional search fees were accompanied by the applicant's protest.   |   |
| 1-10  Remark on Protest  The additional search fees were accompanied by the applicant's protest.   | 4. Ty No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is   |
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#### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-10

Mutant R475A, a pharmaceutical composition containing said mutant and its use for gene therapy

2. claims: 1-10

, Mutant R484A, supra

3. claims: 1-10

Mutant R484E, supra-

4. claims: 1-10

Mutant R487A, supra

5. claims: 1-10

Mutant R487E, supra

6. claims: 1-10

Mutant K527A, supra

7. claims: 1-10

Mutant K532A, supra

8. claims: 1-10

Mutant R585E, supra

9. claims: 1-10

Mutant R588E, supra

10. claims: 1-10

### FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Due to the large number of combinatorial possibilities, the total number of inventions has not been determined. However, it is considered that each modification at a certain position and each combination of modifications at more than one position may constitute a separate invention.

ntormation on patent family members

Interplement Application No PC1/EP2004/006222

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